

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 2

### AMENDMENTS TO THE CLAIMS

Please add or amend the claims to read as follows, and cancel without prejudice or disclaimer to resubmission in a divisional or continuation application claims indicated as cancelled:

1. (Currently amended) A method of determining at least one first and second gastro-intestinal conditions in a subject, comprising the steps of:

administering to said subject a test meal comprising a labeled marker whose by-products are absorbed and exhaled in breaths of said subject after exit from the stomach of said subject;

performing on said subject a first breath test selected from a group of breath tests, each breath test of said group providing said gastro-intestinal information related to said subject;

performing on said subject at least a second breath test indicative of at least one of the first and the second selected from said group of breath tests, according to the outcome of at least said first breath test gastro-intestinal conditions; and

determining the first and the second gastro-intestinal conditions in said subject from the outcome of at least one of said first and said second breath tests a gastro-intestinal condition of said subject.

2. (Original) A method according to claim 1 and wherein said condition comprises at least one of dyspepsia and irritable bowel syndrome.

3. (Currently amended) A method according to claim 2-1 and wherein said condition includes \_\_\_\_\_ dyspepsia \_\_\_\_\_ arises from at least one of a gastric emptying disorder, a gastric accommodation disorder, and a *Helicobacter pylori* infection.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 3

4. (Currently amended) A method according to claim 2-1 and wherein said irritable bowel condition includes ~~syndrome arises from~~ at least one of a sugar malabsorption disorder, a bacterial overgrowth, and an orececal transit time disorder.
5. (Original) A method according to claim 4 and wherein said sugar malabsorption disorder is at least one of lactose intolerance, fructose, intolerance, sucrose intolerance and maltose intolerance.
6. (Withdrawn) A substrate for isotopic breath tests, comprising an isotopically labeled material in a micro-encapsulated coating material, wherein the properties of the micro-encapsulation coating material are chosen such that said isotopically labeled material is released in a predetermined part of the gastro-intestinal tract.
7. (Withdrawn) A substrate according to claim 6 and wherein said micro-encapsulation coating material is chosen such that it breaks down and releases the isotopically labeled material according to the pH value of the environment through which it is passing.
8. (Withdrawn) A substrate according to claim 7 and wherein said micro-encapsulation coating material is chosen such that it breaks down and releases the isotopically labeled material only after leaving the stomach of a subject.
9. (Withdrawn) A substrate according to claim 8 and wherein said isotopically labeled material is used as a marker for determining passage through the duodenum.
10. (Withdrawn) A substrate according to claim 6 and wherein said micro-encapsulation coating material is chosen such that it breaks down and releases the isotopically

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 4

labeled material under the effect of enzymic action arising from the enzymic environment through which it is passing.

11. (Withdrawn) A substrate according to claim 10 and wherein said enzymes are those secreted by at least one of the pancreas and the gall bladder, such that said isotopically labeled material is used as a marker for determining passage through the duodenum.
12. (Withdrawn) A substrate according to claim 6 and wherein said micro-encapsulation coating is such that it can be more readily bonded to an administered meal than said isotopically labeled material.
13. (Original) A method of performing a breath test for the determination of gastric emptying of a subject, comprising the steps of:  
administering to said subject a test meal comprising a labeled marker whose by-products are absorbed and exhaled in breaths of said subject after exit from the stomach of said subject;  
calculating in real time, as the breath test proceeds, at least one of the  $t_{1/2}$ ,  $t_{lag}$ , delta over baseline (DoB), and Gastric Emptying Coefficient (GEC) parameters of said subject;  
determining by means of extrapolation to within allowed error limits, a final estimated value of at least one of said parameters; and  
determining if at least one of said parameters departs significantly from predetermined averaged norms of said parameters obtained from many test subjects.
14. (Original) A method according to claim 13, and wherein an indication is provided of a gastric emptying disorder in said subject while said subject is still providing exhaled breath samples.
15. (Original) A method according to claim 13, and wherein an indication is provided of a gastric emptying disorder in said subject in accordance with the on-going analyses of said breaths of said subject.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 5

16. (Original) A method for the determination of gastric accommodation in a subject, comprising the steps of:
  - administering to said subject a first liquid meal comprising a first predetermined volume;
  - determining at least one characteristic of emptying of said first meal from the stomach of said subject;
  - administering to said subject a second liquid meal comprising a second predetermined volume greater than the predetermined first volume;
  - determining at least one characteristic of emptying of said second meal from the stomach of said subject; and
  - determining the gastric accommodation of the subject according to the deviation between said at least one emptying characteristic of said second meal and said at least one emptying characteristic of said first meal.
17. (Original) A method according to claim 16 and wherein said second predetermined volume is sufficient to cause gastric distension in said subject.
18. (Original) A method according to claim 16 and wherein said second predetermined volume is at least 750 milliliters of liquid.
19. (Original) A method according to claim 16 and wherein at least one of said first and said second liquid meal has a predetermined gastric retention characteristic arising from at least one of a predetermined pH, a predetermined calorific value and a predetermined composition of said liquid meal.
20. (Original) A method according to claim 19 and wherein said predetermined pH is less than 3.0.
21. (Original) A method according to claim 20 and wherein said predetermined calorific value is at least 200 kilocalories.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 6

22. (Original) A method according to claim 20 and wherein said predetermined composition is an isotonic composition.
23. (Original) A method according to claim 16 and wherein said administering to said subject of said second liquid meal is performed as soon as said at least one emptying characteristic of said first meal from the stomach of said subject is determined.
24. (Original) A method according to claim 16 and wherein said administering to said subject of said second liquid meal is performed after a time when essentially all physiological effects of said first meal on said subject have terminated.
25. (Original) A method according to claim 24 and wherein said administering to said subject of said second liquid meal is performed on a successive day to said first meal.
26. (Original) A method according to claim 16 and wherein said determining said rate of emptying is performed by one of a breath test, scintigraphy, an X-ray, computerized tomography, gamma imaging and an ultrasound method.
27. (Original) A method for the determination of gastric accommodation in a subject, comprising the steps of:
  - administering to said subject a liquid meal comprising a predetermined volume, at least one average gastric emptying characteristic of said meal for a large plurality of normal subjects being known;
  - determining said at least one emptying characteristic of said meal from the stomach of the subject; and
  - determining the gastric accommodation of the subject according to the deviation between said at least one emptying characteristic of said meal from the stomach of said subject and said at least one average emptying characteristic of said meal for a large plurality of normal subjects.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 7

28. (Original) A method according to claim 27 and wherein said predetermined volume is sufficient to cause gastric distension in said subject.
29. (Original) A method according to claim 27 and wherein said predetermined volume is at least 750 milliliters of liquid.
30. (Original) A method according to claim 27 and wherein said liquid meal has a gastric retention characteristic arising from at least one of a predetermined pH, a predetermined calorific value and a predetermined composition of said liquid meal.
31. (Original) A method according to claim 30 and wherein said predetermined pH is less than 3.0.
32. (Original) A method according to claim 31 and wherein said predetermined calorific value is at least 200 kilocalories.
33. (Original) A method according to claim 31 and wherein said predetermined composition is an isotonic composition.
34. (Original) A method according to claim 27 and wherein said determining said rate of emptying is performed by one of a breath test, scintigraphy, an X-ray, computerized tomography, gamma imaging and an ultrasound method.
35. (Original) A breath test for determining the effect of the volume of a meal on the intragastric pressure, comprising the steps of:
  - administering to said subject an isotopically labeled liquid meal comprising a predetermined volume and having a predetermined gastric retention characteristic;
  - monitoring the emptying of said meal from the stomach of said subject by means of a breath test performed for isotopically labeled breath; and
  - monitoring said emptying as a function of remaining gastric volume.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 8

36. (Original) A method according to claim 35 and wherein said determining said rate of emptying is performed by one of a breath test, scintography, an X-ray, computerized tomography, gamma imaging and an ultrasound method.
37. (Original) A method for the determination of gastro-intestinal disorders in a subject, comprising the steps of:
  - administering to the subject a meal comprising at least two marker materials, a first material which is generally not absorbed in the subject's stomach, and which releases a gas in the presence of bacteria, and a second material operative to indicate location of said meal within the gastro-intestinal tract of the subject;
  - detecting the generation of said gas in said subject by means of a breath test; and
  - determining the position within the subject's gastro-intestinal tract at which said gas is generated by means of said second marker material.
38. (Original) A method according to claim 37, and wherein said gas is hydrogen.
39. (Original) A method according to claim 38, and wherein a by-product of said second marker material is also detected by means of a breath test, such that the position of said hydrogen generation in the gastro-intestinal tract of said subject is determined by the temporal relationship between the appearance of hydrogen and of a by-product of said marker material in said subject's breath.
40. (Original) A method according to claim 39, and wherein said second marker material is labeled with a carbon isotope, and said by-product is isotopically labeled carbon dioxide.
41. (Original) A method according to claim 38, and wherein said first material is a sugar metabolized in the small intestine of said subject, such that the time of detection of hydrogen relative to the time of detection of the second marker material is used to determine the presence of bacterial overgrowth in said small intestine.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 9

42. (Original) A method according to claim 41, and wherein said second material is a labeled sugar also metabolized in the small intestine of said subject, such that the generally concurrent appearance in the breath of said subject of hydrogen and a by-product of said second marker material is indicative of the presence of bacterial overgrowth in said subject.
43. (Original) A method according to claim 41, and wherein said second material is a labeled sugar also metabolized in the small intestine of said subject, such that the appearance in the breath of said subject of a by-product of said second marker material significantly prior to the appearance of hydrogen is generally indicative of the absence of bacterial overgrowth in said subject.
44. (Original) A method according to claim 41 and wherein said first material is at least one of glucose and lactulose.
45. (Original) A method according to claim 41, and wherein said second material is at least one of labeled sodium acetate, sodium octanoate, glucose, a probe such as acetyl leucine, or a microencapsulated labeled substrate
46. (Original) A method according to claim 38, and wherein said first material is a sugar generally not metabolized in the small intestine of said subject, such that the time of detection of hydrogen relative to the time of detection of said second marker material is used to determine the oro-caecal transit time of said subject.
47. (Original) A method according to claim 38, and wherein said first material is a sugar of a group thought to be malabsorbed in the small intestine of said subject, such that it arrives essentially unabsorbed at the colon of said subject, where hydrogen is generated by the presence of colonic bacteria, such that the time of detection of hydrogen relative to the time of detection of the second marker material is used to determine a sugar intolerance in said subject.



APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 10

48. (Original) A method according to claim 47, and wherein said second material is an isotopically labeled material generally absorbed in the colon, such that the time of detection of hydrogen relative to the time of detection of said second marker material is used to determine a sugar intolerance in said subject.
49. (Original) A method according to claim 48, and wherein said second material is xylose labeled with a carbon isotope, and said by-product is isotopically labeled carbon dioxide.
50. (Original) A method according to claim 47, and wherein said second material is an isotopically labeled material generally absorbed in the small intestine, such that the relative time and quantity of detection of hydrogen and labeled by-products of said second marker material is used to determine whether said subject is suffering from one or both of a sugar intolerance and a bacterial overgrowth.
51. (Original) A method according to claim 50, and wherein the time of detection of hydrogen, characteristic of a part of said first material in the presence of bacteria, relative to the time of detection of said labeled by-products of said second marker material is used to determine that said subject is suffering a bacterial overgrowth.
52. (Original) A method according to claim 50, and wherein the detection of hydrogen later than the detection of said labeled by-products of said second marker material indicates that said subject is suffering from a sugar intolerance.
53. (Original) A method according to claim 50, and wherein the time of detection of a first quantity of hydrogen, characteristic of said first material in the presence of bacteria, relative to the time of detection of said labeled by-products of said second marker material is used to determine that said subject is suffering a sugar intolerance and a bacterial overgrowth.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 11

54. (Original) A method according to claim 47 and wherein said sugar is at least one of the group consisting of lactose, fructose, maltose and sucrose.

55. (Original) A method according to claim 37, and wherein a by-product of said second marker material is also detected by means of a breath test, such that the position of said hydrogen generation in the gastro-intestinal tract of said subject is determined by the temporal relationship between the appearance of hydrogen and of a by-product of said marker material in said subject's breath.

56. (Original) A method according to claim 55, and wherein said second marker material is labeled with a carbon isotope, and said by-product is isotopically labeled carbon dioxide.

57. (Original) A method according to claim 37, and wherein said first material is a sugar metabolized in the small intestine of said subject, such that the time of detection of hydrogen relative to the time of detection of the second marker material is used to determine the presence of bacterial overgrowth in said small intestine.

58. (Original) A method according to claim 57, and wherein said second material is a labeled sugar also metabolized in the small intestine of said subject, such that the generally concurrent appearance in the breath of said subject of hydrogen and a by-product of said second marker material is indicative of the presence of bacterial overgrowth in said subject.

59. (Original) A method according to claim 57, and wherein said second material is a labeled sugar also metabolized in the small intestine of said subject, such that the appearance in the breath of said subject of a by-product of said second marker material significantly prior to the appearance of hydrogen is generally indicative of the absence of bacterial overgrowth in said subject.

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 12

60. (Original) A method according to claim 57 and wherein said first material is at least one of glucose and lactulose.

61. (Original) A method according to claim 57, and wherein said second material is at least one of labeled sodium acetate, sodium octanoate, glucose, a probe such as acetyl leucine, or a microencapsulated labeled substrate.

62. (Original) A method according to claim 37, and wherein said first material is a sugar generally not metabolized in the small intestine of said subject, such that the time of detection of hydrogen relative to the time of detection of said second marker material is used to determine the oro-caecal transit time of said subject.

63. (Original) A method according to claim 37, and wherein said first material is a sugar of a group thought to be malabsorbed in the small intestine of said subject, such that it arrives essentially unabsorbed at the colon of said subject, where hydrogen is generated by the presence of colonic bacteria, such that the time of detection of hydrogen relative to the time of detection of the second marker material is used to determine a sugar intolerance in said subject.

64. (Original) A method according to claim 63, and wherein said second material is an isotopically labeled material generally absorbed in the colon, such that the time of detection of hydrogen relative to the time of detection of said second marker material is used to determine a sugar intolerance in said subject.

65. (Original) A method according to claim 64, and wherein said second material is xylose labeled with a carbon isotope, and said by-product is isotopically labeled carbon dioxide.

66. (Original) A method according to claim 63, and wherein said second material is an isotopically labeled material generally absorbed in the small intestine, such that

APPLICANT(S): Ben-Oren, Ilan et al

SERIAL NO.: 10/784,117

FILED: February 20, 2004

Page 13

the relative time and quantity of detection of hydrogen and labeled by-products of said second marker material is used to determine whether said subject is suffering from one or both of a sugar intolerance and a bacterial overgrowth.

67. (Original) A method according to claim 66, and wherein the time of detection of hydrogen, characteristic of a part of said first material in the presence of bacteria, relative to the time of detection of said labeled by-products of said second marker material is used to determine that said subject is suffering a bacterial overgrowth.

68. (Original) A method according to claim 66, and wherein the detection of hydrogen later than the detection of said labeled by-products of said second marker material indicates that said subject is suffering from a sugar intolerance.

69. (Original) A method according to claim 66, and wherein the time of detection of a first quantity of hydrogen, characteristic of said first material in the presence of bacteria, relative to the time of detection of said labeled by-products of said second marker material is used to determine that said subject is suffering a sugar intolerance and a bacterial overgrowth.

70. (Original) A method according to claim 63 and wherein said sugar is at least one of the group consisting of lactose, fructose, maltose and sucrose.

71. (New) A method according to claim 1, wherein determining of said second gastrointestinal condition is based on the evaluation of said first gastrointestinal condition.